

WHAT IS CLAIMED IS:

1. An isolated polynucleotide encoding an alpha-2A adrenergic receptor molecule comprising SEQ ID NO: 1 or 2 or fragment or complement thereof, wherein the polynucleotide comprises at least one polymorphic site.
2. The polynucleotide of claim 1, wherein the polymorphic site comprises cytosine or guanine at nucleotide position 753 of SEQ ID NO: 1 or 2.
3. The polynucleotide of claim 1, wherein the polymorphic site occurs in human chromosome 10.
4. An isolated alpha-2A adrenergic receptor gene product comprising SEQ ID NO: 3 or 4 or fragment thereof, wherein the gene product comprises at least one polymorphic site.
5. The gene product of claim 4, wherein the polymorphic site comprises lysine or asparagine at amino acid position 251 of SEQ ID NO: 3 or 4.
6. An oligonucleotide comprising from about 10 to about 50 nucleotides that hybridize with a region upstream of nucleotide position 753 of SEQ ID NO: 1 or 2 or complementary sequence thereof, and wherein the oligonucleotide does not hybridize with nucleotide position 753 of SEQ ID NO: 1 or 2 or complementary sequence thereof.
7. An oligonucleotide comprising from about 10 to about 50 nucleotides that hybridize with a region downstream of nucleotide position 753 of SEQ ID NO: 1 or 2 or complementary sequence thereof, and wherein the oligonucleotide does not hybridize with nucleotide position 753 of SEQ ID NO: 1 or 2 or complementary sequence thereof.
8. The oligonucleotide of claim 6, wherein the oligonucleotide is hybridized immediately adjacent to nucleotide position 753 of SEQ ID NO: 1 or 2 or complementary sequence thereof.

9. The oligonucleotide of claim 7, wherein the oligonucleotide is hybridized immediately adjacent to nucleotide position 753 of SEQ ID NO: 1 or 2 or complementary sequence thereof.

10. The oligonucleotide of claim 8, wherein the oligonucleotide is a primer oligonucleotide.

11. The oligonucleotide of claim 9, wherein the oligonucleotide is a primer oligonucleotide.

12. An oligonucleotide comprising a nucleotide sequence complementary to a region of SEQ ID NO: 1 or 2 or fragment thereof that encode an alpha-2A adrenergic receptor molecule and which, when hybridized to the region permit identification of at least one polymorphic site.

13. The oligonucleotide of claim 12, wherein the polymorphic site comprises cytosine or guanine at nucleotide position 753 of SEQ ID NO: 1 or 2.

14. The oligonucleotide of claim 12, wherein the oligonucleotide comprises from about 10 to about 50 nucleotides.

15. The oligonucleotide of claim 12, wherein the oligonucleotide is an allele-specific oligonucleotide.

16. The oligonucleotide of claim 12, wherein the oligonucleotide is a primer oligonucleotide.

17. The oligonucleotide of claim 12, wherein the oligonucleotide is a primer oligonucleotide selected from the group consisting of
5'-TTTACCCATCGGCTCTCCCTAC-3' (SEQ ID NO: 5);
5'-GAGACACCAGGAAGAGGTTTGG-3' (SEQ ID NO: 6);
5'-TCGTCATCATCGCCGTGTTC-3' (SEQ ID NO: 7);
5'-CGTACCACTTCTGGTCGTTGATC-3' (SEQ ID NO: 8);
5'-GCCATCATCATCACCGTGTGGGTC-3' (SEQ ID NO: 9);
5'-GGCTCGCTCGGGCCTTGCTTTG-3' (SEQ ID NO: 10);

5'-GACCTGGAGGAGAGCTCGTCTT-3' (SEQ ID NO: 11);
5'-TGACCGGGTTCAACGAGCTGTTG-3' (SEQ ID NO: 12);
5'-GCCACGCACGCTCTTCAAATTCT-3' (SEQ ID NO: 13);
5'-TTCCCTTGTAGGAGCAGCAGAC-3' (SEQ ID NO: 14);
5 5'-TGTAACACGACGGCCAGT-3' (SEQ ID NO: 15);
5'-CAGGAAACAGCTATGACC-3' (SEQ ID NO: 16) and complementary
sequences thereof.

18. The allele-specific oligonucleotide of claim 15, wherein the
oligonucleotide is complementary to cytosine or guanine at nucleotide position 753 of
10 SEQ ID NO: 1 or 2.

19. The oligonucleotide of claim 15, wherein the allele-specific
oligonucleotide is labeled with a label selected from the group consisting of
radiolabel, fluorescent label, bioluminescent label, chemiluminescent label, nucleic
acid label, hapten label, and enzyme label.

15 20. A primer oligonucleotide for polymerase-mediated extension
comprising at least one polymorphic site of SEQ ID NO: 1 or 2, wherein polymerase-
mediated extension of the primer amplifies the polymorphic site.

21. The primer oligonucleotide of claim 20, wherein the polymorphic site
comprises cytosine or guanine at nucleotide position 753 of SEQ ID NO: 1 or 2.

20 22. The primer oligonucleotide of claim 20, wherein the primer comprises
a nucleotide sequence from about 10 to about 50 nucleotides.

23. A kit for detecting at least one polymorphism in nucleic acids encoding
an alpha-2A adrenergic receptor molecule comprising a container having an
oligonucleotide comprising a region of SEQ ID NO: 1 or 2 or complement thereof for
25 detecting the polymorphism.

24. The kit of claim 23, wherein the oligonucleotide comprises a
nucleotide sequence from about 10 to about 50 nucleotides.

25. A kit for detecting at least one polymorphism in nucleic acids encoding an alpha-2A adrenergic receptor molecule comprising a container having at least two primers for amplifying SEQ ID NO: 1 or 2 or fragment or complement thereof and at least one detection primer for detecting the polymorphism.

5 26. The kit of claim 25, wherein the amplification primers are primers selected from the group consisting of 5'-TTACCCATCGGCTCTCCCTAC-3' (SEQ ID NO: 5); 5'-GAGACACCAGGAAGAGGTTTTGG-3' (SEQ ID NO: 6);
5'-TCGTCATCATCGCCGTGTTC-3' (SEQ ID NO: 7);
5'-CGTACCACTTCTGGTCGTTGATC-3' (SEQ ID NO: 8);
10 5'-GCCATCATCATCACCGTGTGGGTC-3' (SEQ ID NO: 9);
5'-GGCTCGCTCGGGCCTTGCCTTTG-3' (SEQ ID NO: 10);
5'-GACCTGGAGGAGAGCTCGTCTT-3' (SEQ ID NO: 11);
5'-TGACCGGGTTCAACGAGCTGTTG-3' (SEQ ID NO: 12);
5'-GCCACGCACGCTCTTCAAATTCT-3' (SEQ ID NO: 13);
15 5'-TTCCCTTGTAGGAGCAGCAGAC-3' (SEQ ID NO: 14);
5'-TGTAACGACGGCCAGT-3' (SEQ ID NO: 15);
5'-CAGGAAACAGCTATGACC-3' (SEQ ID NO: 16) and complementary sequences thereof.

20 27. The kit of claim 25, wherein the detection primer comprises a nucleotide sequence from about 10 to about 50 nucleotides.

28. A method of genotyping nucleic acids encoding an alpha-2A adrenergic receptor molecule from a sample comprising performing a primer extension reaction employing an oligonucleotide comprising a region of SEQ ID NO: 1 or 2 or complement thereof.

25 29. The method of claim 28, wherein the primer extension reaction is a single-nucleotide primer extension reaction.

30. The method of claim 28, wherein the oligonucleotide comprises cytosine or guanine at nucleotide position 753 of SEQ ID NO: 1 or 2.

31. The oligonucleotide of claim 28, wherein the oligonucleotide comprises a nucleotide sequence from about 10 to about 50 nucleotides.

32. A method of genotyping nucleic acids encoding an alpha-2A adrenergic receptor molecule from a sample of an individual, comprising:

5 a) isolating from the individual the sample having a polynucleotide encoding the alpha-2A adrenergic receptor molecule comprising SEQ ID NO: 1 or 2 or fragment or complement thereof;

10 b) incubating the polynucleotide with at least one oligonucleotide, the oligonucleotide having a nucleotide sequence that is complementary to a region of the polynucleotide, and which, when hybridized to the region permits the identification of the nucleotide present at a polymorphic site of the polynucleotide, wherein the incubation is under conditions sufficient to allow specific hybridization to occur between complementary nucleic acid molecules;

c) permitting the hybridization to occur; and

15 d) identifying the polymorphic site to obtain the genotype of the individual.

33. The method of claim 32, further comprising amplifying at least one region comprising at least one polymorphic site of the polynucleotide prior to the hybridization.

20 34. The method of claim 32, wherein the hybridization is selected from the group consisting of southern blot, dot blot, reverse dot blot, northern blot, and allele-specific oligonucleotide hybridization.

25 35. The method of claim 32, wherein the oligonucleotide is labeled with a label selected from the group consisting of radiolabel, fluorescent label, bioluminescent label, chemiluminescent label, nucleic acid label, hapten label, and enzyme label.

36. The method of claim 32, wherein the identity of the polymorphic site is determined by dideoxy sequencing, restriction digestion, allele-specific polymerase reaction, single-stranded conformational polymorphism analysis, genetic bit analysis, temperature gradient gel electrophoresis, ligase chain reaction, or
5 ligase/polymerase genetic bit analysis.

37. The method of claim 32, wherein the polymorphic site comprises cytosine or guanine at nucleotide position 753 of SEQ ID NO: 1 or 2.

38. The method of claim 32, wherein the oligonucleotide comprises a nucleotide sequence from about 10 to about 50 nucleotides.

10 39. A method for determining an individual at increased risk for developing a disease associated with an alpha-2A adrenergic receptor molecule which comprises obtaining a sample comprising nucleic acids from the individual and detecting a polymorphism in nucleic acids encoding the alpha-2A adrenergic receptor molecule comprising SEQ ID NO: 1 or 2 or fragment or complement thereof which
15 correlates to the disease thereby identifying the individual at increased risk for the disease.

40. The method of claim 39, wherein the disease is a cardiovascular or a central nervous system disease or combinations thereof.

20 41. The method of claim 39, wherein the alpha-2A adrenergic receptor molecule comprises SEQ ID NO. 3 or 4 or fragment thereof.

42. A method for diagnosing or prognosing an individual with a disease associated with an alpha-2A adrenergic receptor molecule, comprising obtaining a sample comprising nucleic acids from the individual and detecting a polymorphism in nucleic acids encoding the alpha-2A adrenergic receptor molecule comprising SEQ
25 ID NO: 1 or 2 or fragment or complement thereof which correlates to the disease thereby diagnosing or prognosing the disease.

43. The method of claim 42, wherein the disease is a cardiovascular, a central nervous system disease or combinations thereof.

44. The method of claim 37, wherein the alpha-2A adrenergic receptor molecule comprises SEQ ID NO. 3 or 4 or fragment thereof.

45. The method of ~~claim 44~~, wherein the alpha-2A adrenergic receptor molecule comprises lysine or asparagine at amino acid position 251 of SEQ ID NO: 3 or 4.

46. A method of predicting an individual's response to an agonist or antagonist, comprising:

- a) obtaining a sample comprising nucleic acids from the individual;
- b) detecting a polymorphism in the nucleic acids encoding the alpha-2A adrenergic receptor molecule comprising SEQ ID NO: 1 or 2 or fragment or complement thereof; and iii) correlating the polymorphism to a predetermined response thereby predicting the individual's response to the agonist or antagonist.

47. The method of claim 46, wherein the alpha-2A adrenergic receptor molecule comprises SEQ ID NO. 3 or 4 or fragment thereof.

48. The method of claim 47, wherein the alpha-2A adrenergic receptor molecule comprises lysine or asparagine at amino acid position 251 of SEQ ID NO: 3 or 4.

49. The method of claim 46, wherein the agonist is an alpha-2A adrenergic receptor agonist.

50. The method of claim 46, wherein the antagonist is an alpha-2A adrenergic receptor antagonist.

51. The method of claim 49, wherein the alpha-2A adrenergic receptor agonist is an agonist selected from the group consisting of epinephrine, norepinephrine, clonidine, oxymetazoline, guanabenz, UK14304, BHT933 and combinations thereof.

52. The method of claim 50, wherein the alpha-2A adrenergic receptor antagonist is an antagonist selected from the group consisting of yohimbine, prazosin, ARC 239, rauwolscine, idazoxan, tolazoline, phentolamine and combinations thereof.

53. The method of claim 46, wherein the predetermined response to the agonist or antagonist is correlated to adenyly cyclase, MAP kinase activity or inositol phosphate levels.

54. A method for selecting an appropriate pharmaceutical composition to administer to an individual having a disease associated with an alpha-2A adrenergic receptor molecule comprising detecting in a sample a polymorphism in nucleic acids encoding the alpha-2A adrenergic receptor molecule comprising SEQ ID NO: 1 or 2 or fragment or complement thereof in the individual and selecting the appropriate pharmaceutical composition based on the polymorphism present.

55. The method of claim 54, wherein the disease is a cardiovascular disease, a central nervous system disease or combinations thereof.

56. The method of claim 54, wherein the alpha-2A adrenergic receptor molecule comprises SEQ ID NO: 3 or 4 or fragment thereof.

57. The method of claim 56, wherein the alpha-2A adrenergic receptor molecule comprises lysine or asparagine at amino acid position 251 of SEQ ID NO: 3 or 4.

58. The method of claim 54, wherein the pharmaceutical composition is an alpha-2A adrenergic receptor agonist or antagonist.

59. The method of claim 58, wherein the alpha-2A adrenergic receptor agonist is an agonist selected from the group consisting of epinephrine, norepinephrine, clonidine, oxymetazoline, guanabenz, UK14304, BHT933, and combinations thereof.

60. The method of claim 58, wherein the alpha-2A adrenergic receptor antagonist is an antagonist selected from the group consisting of yohimbine, prazosin, ARC 239, rauwolscine, idazoxan, tolazoline, phentolamine and combinations thereof.

5 61. The method of claim 54, wherein the appropriate pharmaceutical composition to administer is correlated to adenyly cyclase, MAP kinase or inositol phosphate activity.

62. A recombinant host cell having a polynucleotide encoding the alpha-2A adrenergic receptor molecule comprising SEQ ID NO: 2.

10 63. The recombinant host cell of claim 62 that expresses SEQ ID NO: 4 or fragment thereof.

64. An expression vector having a polynucleotide encoding an alpha-2A adrenergic receptor molecule comprising SEQ ID NO: 2.

65. The expression vector of claim 64 that expresses SEQ ID NO: 4 or fragment thereof.

15 66. A transgenic animal having incorporated into its genome a polynucleotide comprising SEQ ID NO: 2.

67. The transgenic animal of claim 66, wherein the mammal expresses a gene product comprising SEQ ID NO: 4 or fragment thereof.

20 68. An isolated antibody that binds with an epitope on SEQ ID NO: 4 or fragment thereof.

69. The isolated antibody of claim 68, wherein the epitope comprises lysine at amino acid position 251 of SEQ ID NO: 4.